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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,766	06/06/2005	Yasuki Itoh	081356-0242	5454

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EXAMINER	
WALLENHORST, MAUREEN	
ART UNIT	PAPER NUMBER
1797	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,766	ITOH ET AL.	
	Examiner	Art Unit	
	Maureen M. Wallenhorst	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-27 and 29-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-27 and 29-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/30/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

2. Claims 25-27 and 29-36 are objected to because of the following informalities: In part (i) of claims 25 and 27, the word "polyoxyetylene" is misspelled. In part (ii) of claim 25, the word "destran" is misspelled. Appropriate correction is required.

3. Claims 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

On line 2 of claim 19, the phrase "the monovalent cation" lacks antecedent basis since claim 19 depends from claim 15. In order for this phrase to have proper antecedent basis, claim 19 should depend from claim 16.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Sugiuchi (WO 00/17388, English language equivalent is US 6,794,157).

Sugiuchi teaches of a kit for the determination of both HDL and LDL cholesterol that comprises a reagent for aggregating lipoproteins, and a reagent comprising a combination of cholesterol esterase and cholesterol oxidase. The reagent comprising both cholesterol enzymes can be used to measure low-density lipoproteins. The reagent for aggregating lipoproteins is the combination of a divalent metal salt and at least one member selected from the group consisting of heparin, phosphotungstic acid, dextran sulfuric acid and polyethylene glycol (PEG). The kit also contains a reagent comprising a polyoxyethylene derivative which enables the enzymes to act only on LDL cholesterol. The polyoxyethylene derivative can be a polyoxyethylene alkyl ether or a polyoxyethylene alkylaryl ether, such as those recited in instant claims 25 and 27. Therefore, the kit taught by Sugiuchi contains all of the components recited in the kit of instant claims 25 and 27-28, namely a separation agent that includes a polyanion and a divalent cation or a separation agent that includes polyethylene glycol, and a reagent for measuring low-density lipoprotein. See claims 21-22 and 24-25 in US Patent 6,794,157.

7. Claims 1, 3-6 and 15-19 are rejected under 35 U.S.C. 102(b) as being anticipated by JP 07294532 (submitted in the Information Disclosure Statement filed on June 6, 2005).

JP 07294532 teaches of a method for the fractionation and measurement of low specific gravity serum lipoprotein based upon precipitation of the lipoprotein in the serum with a polyanion such as dextran sulfate, a divalent cation such as calcium, magnesium or manganese, and a monovalent cation such as sodium or potassium. JP 07294532 teaches that by adjusting the concentrations of the polyanion, divalent cation and monovalent cation in the reagent,

different lipoprotein fractions including LDL, VLDL and chylomicrons are selectively and separately precipitated and measured by nephelometry. JP 07294532 also teaches that the lipids and lipoproteins remaining in the supernatant after precipitation of the blood sample are measured. Since the same reagents as used in the instant invention (i.e. a polyanion, a divalent cation and a monovalent cation) are used in the method taught by JP 07294532 for precipitating lipoprotein fractions from a blood sample, the supernatant resulting after precipitation of LDL, VLDL and chylomicrons would inherently contain both HDL and small particle LDL therein, as in the instant invention, and JP 07294532 discloses measuring these supernatant lipoprotein fractions. The cholesterol, triglyceride and protein portions of each lipoprotein fraction in both the precipitate and the supernatant are separately determined. Thus, the teaching of JP 07294532 inherently anticipates claims 1, 3-6 and 15-19. See paragraph 0017 and the claims in the English language machine translation of JP 07294532 included with this Office action.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 7-9, 12-14 and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 07294532. For a teaching of JP 07294532, see previous paragraphs in this Office action.

JP 07294532 fails to teach of the final concentrations of the polyanion, divalent cation and monovalent cation used to precipitate LDL, VLDL and chylomicrons from a blood sample, and fails to teach that the lipoprotein fractions remaining in the supernatant of the sample are selectively measured for either cholesterol, triglycerides or with an apoprotein B antibody. However, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to vary the concentrations of the polyanion, divalent cation and monovalent cation used to precipitate LDL, VLDL and chylomicrons from a blood sample in the method taught by JP 07294532 to the levels recited in the instant claims since in the absence of any unexpected results, concentration is a result effective parameter that can be experimentally varied in order to achieve optimum results for a particular procedure. In addition, it would have been obvious to one of ordinary skill in the art to measure the lipoprotein fractions remaining in the supernatant of the sample analyzed in the method taught by JP 07294532 by selectively measuring either cholesterol, triglycerides or with the use of an apoprotein B antibody since each of these techniques are readily known to one of skill in the art, and the use of any of these techniques for the measurement of the lipoprotein fractions in the supernatant would yield predictable results.

11. Claims 10-11 and 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 07294532 in view of Sugiuchi (WO 00/17388, English language translation is US 6,794,157). For a teaching of both JP 07294532 and Sugiuchi, see previous paragraphs in this Office action.

The primary reference to JP 07294532 fails to teach that the different lipoprotein fractions in a serum sample can be selectively precipitated and measured by combining the serum sample with a reagent comprising polyethylene glycol. However, based upon the combination of JP 07294532 and Sugiuchi, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute polyethylene glycol (PEG) for the polyanion in the composition taught by JP 07294532 used for selectively precipitating lipoprotein fractions in a serum sample since Sugiuchi teaches that PEG is a known aggregating agent for aggregating lipoproteins in a serum sample that acts equivalently to a polyanion such as dextran sulfate.

12. Claims 26 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sugiuchi (WO 00/17388, English language translation is US 6,794,157) in view of JP 07294532. For a teaching of both Sugiuchi and JP 07294532, see previous paragraphs in this Office action.

The primary reference to Sugiuchi fails to teach that the reagent for aggregating lipoproteins in the kit also includes a monovalent cation therein in addition to the polyanion and the divalent cation. However, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to include a monovalent cation in the aggregating reagent taught in the kit of Sugiuchi since JP 07294532 teaches that a monovalent cation in a composition also including a polyanion and a divalent cation serves to help adjust the ionic strength of the sample.

13. Claims 30-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sugiuchi (WO 00/17388, English language translation is US 6,794,157). For a teaching of Sugiuchi, see previous paragraphs in this Office action.

Sugiuchi fails to teach of the volumes of the polyanion and divalent cation included in the reagents of the kit, and the volume of these reagents added to a test sample. However, it would have been obvious to one of ordinary skill in the art to adjust the volumes of the polyanion and divalent cation included in the reagents of the kit taught by Sugiuchi to the volumes recited in instant claims 30-36, and to adjust the volume of the reagents in the kit taught by Sugiuchi added to a test sample to the ratios set forth in instant claims 30-36 since in the absence of any unexpected results, the volume of a reagent either included in a composition or added to a test sample is a result effective parameter that can be experimentally varied in order to achieve optimum results for a particular procedure.

14. Applicant's arguments filed October 15, 2007 have been fully considered but they are not persuasive.

The previous objection to the abstract made in the last Office action mailed on May 15, 2007 has been withdrawn in view of Applicants' amendments to the abstract. In addition, the previous objection to the claims for being improper multiply dependent, and the previous rejection of the claims under 35 USC 112, second paragraph have been withdrawn in view of Applicants' amendments to the claims. However, claims 25-27 and 29-36 are newly objected to, and claim 19 is newly rejected under 35 USC 112, second paragraph, as set forth above, as necessitated by the amendments to the claims.

The previous rejection of the claims under 35 USC 102(a) as being anticipated by Hirano et al, and the previous rejection of the claims under 35 USC 102(a) as being anticipated by JP 2003028882 have been withdrawn in view of the English language translation of the foreign priority document, which establishes the priority date of the instant application as December 6,

2002. The previous rejection of the claims under 35 USC 102(b) as being anticipated by both Miyauchi et al and Griffin et al have been withdrawn in view of the amendments made to the claims.

Applicants argue the rejection of the claims under 35 USC 102(b) and 35 USC 103 as being anticipated by or obvious in view of Sugiuchi by stating that the kit claims have been amended to include a surface active agent such as polyoxyethylene lauryl ether therein, and Sugiuchi does not teach of a kit comprising a surface active agent. This argument is not found persuasive since the kit taught by Sugiuchi includes therein a polyoxyethylene alkyl ether, which enables the cholesterol enzymes in the kit to act only on LDL cholesterol. See lines 8-21 in column 7 and claims 21-22 in Sugiuchi (US 6,794,157, English language translation of WO 00/17388). A polyoxyethylene alkyl ether serves as a surface active agent in the same context as the surface active agents recited in instant claims 25 and 27 since each of the surface active agents recited in these claims are polyoxyethylene alkyl ethers.

Applicants argue the rejection of the claims under 35 USC 102(b) as being anticipated by or obvious in view of JP 07294532 by stating that the instant invention is directed to separating and quantifying small particle LDL or LDL of a high specific gravity in a test sample, whereas JP 07294532 does not relate to small particle LDL since the method of JP 07294532 separates and quantifies low specific gravity serum lipoprotein. In response to this argument, it is noted that JP 07294532 teaches of a method whereby a blood sample is combined with a reagent comprising a polyanion, a divalent cation and a monovalent cation in order to precipitate out LDL, VLDL and chylomicrons from the sample. JP 07294532 teaches that both the precipitate and the supernatant are then analyzed for the lipoproteins contained therein. Since the method of

JP 07294532 uses the same reagent materials (i.e. a polyanion, a divalent cation and a monovalent cation) as used in the instant invention to treat a blood test sample, the lipoproteins other than small particle LDL and HDL are inherently separated out from the small particle LDL and HDL in the precipitate portion of the sample while the small particle LDL and HDL remain behind in the supernatant. Since JP 07294532 then teaches to analyze the supernatant portion for the lipoproteins therein, the teaching of this reference inherently anticipates instant claims 1, 3-6 and 15-19. One of ordinary skill in the art would expect that when a blood test sample is treated with the same reagents (i.e. a polyanion, a divalent cation and a monovalent cation) as used in the instant invention, the same results would occur (i.e. all lipoproteins with the exception of small particle LDL and HDL would be precipitated while the small particle LDL and HDL would remain behind in the supernatant to be analyzed). See the English language machine translation of JP 07294532 included with this Office action.

For all of the above reasons, Applicants' arguments are not found persuasive.

It is noted that on the Information Disclosure Statement filed on May 30, 2007, reference B5 is crossed out since this reference was already considered and made of the record on the PTO-892 form attached to the Office action mailed on May 15, 2007.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maureen M. Wallenhorst whose telephone number is 571-272-1266. The examiner can normally be reached on Monday-Thursday from 6:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden, can be reached on 571-272-1266. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maureen M. Wallenhorst
Primary Examiner
Art Unit 1797

mmw

December 11, 2007

Maureen M. Wallenhorst
MAUREEN M. WALLENHORST
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